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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/561,144	10/17/2006	Iichirou Shimomura	64656 (46590)	9423

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EXAMINER	
LEE, JAE W	

ART UNIT	PAPER NUMBER
1656	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/561,144	SHIMOMURA ET AL.	
	Examiner	Art Unit	
	JAE W. LEE	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 April 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15,18-28,31-38,41,42 and 45-54* is/are pending in the application.

4a) Of the above claim(s) *1-15,18-28,33-38,41,42 and 45-51* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *31,32 and 52-54* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Application status

In response to the previous Office action, a non-Final rejection (mailed on 09/19/2007), Applicants filed a response and amendment received on 04/17/2008. Said amendment canceled Claims 16, 17, 29, 30, 39, 40, 43 and 44, amended Claims 31, and added Claims 52-54. Thus, Claims 31, 32 and 52-54 are at issue and present for examination.

Applicants' arguments filed on 04/17/2008, have been fully considered, and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

The text of those sections of Title 35 U.S. Code not included in the instant action can be found in a prior Office action.

It is noted by the Examiner that Claims 1-15, 18-28, 33-38, 41, 42 and 45-51 are withdrawn from further consideration by the Examiner, 37 CFR 1.142(b) as being drawn to a non-elected invention in the previous Office actions, a non-Final rejection (mailed on 09/19/2007).

Objections to the Specification

The previous objection of the abstract for failing to describe what is new in the art to which the invention pertains, is withdrawn by virtue of Applicants' amendment.

The previous objection of the title of the invention is withdrawn by virtue of Applicants' amendment.

The previous objection of the specification for containing embedded hyperlinks is withdrawn by virtue of Applicants' amendment.

Claim Objections

Claim 31 objected to because of the following informalities:

Claim 31 recites the phrase, "disease involved in differentiation of skeletal muscle cell and/or metabolic abnormality," which can be improved with respect to form. The Examiner suggests replacing the noted phrase with ---disease associated with abnormal differentiation of skeletal muscle cell and/or metabolic abnormality--- or ---disease which results from abnormal differentiation of skeletal muscle cell and/or metabolic abnormality---.

Appropriate correction is required.

Claim Rejections - 35 U.S.C. § 112

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The previous rejection of Claims 31 and 32 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the

subject matter which applicant regards as the invention, is withdrawn by virtue of Applicants' amendment wherein Applicants have inserted active step of bringing a protein comprising an amino acid sequence having an identity of 80% or more to the amino acid sequence of SEQ ID NO: 2 into contact with its receptor in the presence or absence of a test substance.

Claims 31, 32 and 52-54 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 31, 32 and 52-54 recite the phrase, "80% or more to the amino acid sequence starting at amino acid No. 1 in the amino acid sequence shown by SEQ ID NO: 2 or 4," which is unclear and indefinite. It is unclear because whether the phrase is limiting the reference sequence to amino acids 1-104 of SEQ ID NO: 2 and amino acids 1-101 of SEQ ID NO: 4, or if the phrase is limiting the reference sequence to any amino acid sequence which starts at amino acid No. 1 of SEQ ID NO: 2 or 4. If their intended reference sequence is the entire sequence from amino acids 1-104 of SEQ ID NO:2 and the entire amino acid sequence from amino acids 1-101 of SEQ ID NO:4, it is suggested that the phrase be amended to recite, for example, ---identity of 80% or more to amino acids 1-104 of SEQ ID NO:2, or to aminio acids 1-101 of SEQ ID NO:4---. In the interest of advancing prosecution, the noted phrase is interpreted to encompass any amino acid sequence which has 80% or more sequence homology to SEQ ID NO: 2 or 4, wherein said amino acid sequence starts at amino acid No. 1 of SEQ ID NO: 2 or 4.

Claims 31, 32 and 52-54 recite the phrase, "SEQ ID NO: 2 or 4, or a salt thereof, into contact," which is unclear and indefinite. It is unclear whether the phrase "salt thereof" refers to the protein being brought in contact with the receptor, or if refers to the polypeptides of SEQ ID NO:2 or 4. It appears that Applicants could fix this by amending the claim to recite "bringing a protein, or a salt thereof, comprising an amino acid..." In the interest of advancing prosecution, the noted phrase is interpreted as "bringing a protein, or a salt thereof, comprising an amino acid…"

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The previous rejection of Claims 31, 32, 52 and 54 are rejected under 35 U.S.C. § 112, first paragraph, written description, as failing to comply with the written description requirement is withdrawn by virtue of Applicants' amendment because the genus of amino acid sequences that can be used with the claimed methods is limited to any amino acid sequence having 80% or more sequence homology to SEQ ID NO: 2 or 4, wherein said amino acid sequence starts at amino acid No. 1 of SEQ ID NO: 2 or 4.

Claims 31, 32, 52 and 54 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement, because the specification, while being enabling for SEQ ID NO: 2 and 4, does not reasonably provide enablement for

any screening method for a prophylactic/therapeutic substance for a disease involved in differentiation of skeletal muscle cell and/or metabolic abnormality, which comprises bringing a protein or any salt thereof comprising *an amino acid sequence including any fragment and any mutant* having a sequence identity of 80%, optionally 90%, or more to any amino acid sequence starting at Amino Acid No. 1 in the amino acid sequence shown by SEQ ID NO:2 or 4, into contact with its receptor in the presence or absence of a test substance, and selecting the test substance that changes the ability of said protein or *any salt thereof* to bind to said receptor as a candidate for a prophylactic/therapeutic substance for a disease associated with abnormal differentiation of skeletal muscle cell and/or metabolic abnormality as encompassed by the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The rejection was stated in the previous office action as it applied to previous claims 31 and 32. In response to this rejection, Applicants have amended claim 31, and added claims 52-54, and traverse the rejection as it applies to the newly amended claims.

Applicants argue that because of the size of the SS169 protein and known conserved amino acid substitution as stated above, claims 31 and 32 are no longer so broad as to encompass a method of using (1) any protein ~60% sequence homology to SE IDNO.: 2 or 4, (2) any partial peptide, and (3) any salt thereof that may be free of said protein or said partial peptide. A skilled artisan could produce an SS169 variant

that had a homology of 80% or more to the amino acid sequence of SEQ ID NO:2 or 4 and retained physiological activities of SS169 (e.g., suppression of sugar uptake of a skeletal muscle cell upon insulin stimulation, suppression of glycogen synthesis in a skeletal muscle cell and the like) without undue experimentation based on the description of the specification as well as relatively high identity to the amino acid sequence of SEQ ID NO:2 or 4, and known conserved amino acid substitutions. The resulting SS169 variants are able to serve as a useful tool for the development of prophylactic/therapeutic drugs for diseases associated with sugar/lipid metabolic abnormalities as described in the specification, for example, page 84, line 9 to page 85, line 20. Further, Applicants allege that claims that encompass a protein having a homology of 80% or more in some applications have been allowed by the U.S. Patent & Trademark Office, e.g., USP 5,756,671 and USP 6,015,692, in spite of lack of working examples of any variants.

Applicants' arguments have been fully considered but are not deemed persuasive for the following reasons. The scope of the claimed methods are so broad as to encompass any screening method for a prophylactic/therapeutic substance for a disease involved in differentiation of skeletal muscle cell and/or metabolic abnormality, which comprises bringing a protein or any salt thereof comprising *an amino acid sequence including any fragment and any mutant* having a sequence identity of 80%, optionally 90%, or more to any amino acid sequence starting at Amino Acid No. 1 in the amino acid sequence shown by SEQ ID NO:2 or 4, into contact with its receptor in the presence or absence of a test substance, and selecting the test substance that changes

the ability of said protein or *any salt thereof* to bind to said receptor as a candidate for a prophylactic/therapeutic substance for a disease associated with abnormal differentiation of skeletal muscle cell and/or metabolic abnormality. Contrary to Applicants' argument, even in light of the fact that methods of making conservative substitutions were known in the art, claims are not limited to methods of using those amino acid sequences having 80% identity to SEQ ID NO: 2 or 4, wherein all other non-homologous residues are conservative substitutions. Instead, the claims are drawn to methods of using *an amino acid sequence including any fragment and any mutant* having a sequence identity of 80%, optionally 90%, or more to any amino acid sequence starting at Amino Acid No. 1 in the amino acid sequence shown by SEQ ID NO:2 or 4 In addition, although amino acids 1-104 of SEQ ID NO: 2 and amino acids 1-101 of SEQ ID NO:4 are 104 and 101 residues long, respectively, a polypeptide that has 80% identity to the reference sequences recited will comprise a sequence having up to ~21 modifications (alternatively ~11 modifications for 90%).. For example, the genus of variants of SEQ ID NO:2 having 80% sequence identity to amino acids 1-104 of SEQ ID NO: 2 is 104! x 19^{21}/(104-21)!/21!, is a total of 3.65 x 10^{48} variants. In light of the notion that, proteins having very different structures can have the same function (Kisselev et al, 2002), while proteins having very similar structure can have different activities (Witkowski et al, 1999; Wishart et al, 1995), one of skill in the art would not have been able to make and use the claimed invention without further guidance because the disclosure of the specification does not commensurate with the scope of the claimed invention. More importantly, claimed methods encompass any methods

using *any salt thereof*, which means that one of skill in the art has to obtain any protein salt, i.e., protein crystals, as well as any salt that may associate with the protein such as NaCl to carry out the claimed methods. Although one of skill in the art would understand carrying out such methods in a solution, or in an aqueous environment, one would not be able to envision carrying out such methods using said crystals in solid state. Even if one were to carry out such methods in solid state, it requires methods of making protein crystals, which are highly unpredictable. Therefore, it would require undue experimentation for one skilled in the art to practice the claimed methods because the disclosure of the specification is limited to a single representative species of a protein having the amino acid sequence of SEQ ID NO: 2 or 4 that can be used by the claimed method. Further, Applicants' argument that USPTO has previously allowed "80% homology" language in USP 5,756,671 and USP 6,015,692, is not deemed persuasive because the instant application has been examined according to the current guidelines set forth by the USPTO and the MPEP. It is also noted that each application is examined on its own merits and any discussion in regard to the prosecution of other patent applications would be improper herein since it will require a detailed review of the record in each case. For the reasons provided herein and in the previous office action, the rejection under this statute is maintained.

The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of a protein comprising *an amino acid sequence including any fragment and any mutant* having an identity of 80%, optionally 90%, or more to the amino acid

sequence starting at Amino Acid No. 1 in the amino acid sequence shown by SEQ ID NO:2 or 4, *or any salt thereof* used in the claimed methods having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim Rejections - 35 U.S.C. § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 31, 32 and 52-54 are rejected under 35 U.S.C. § 102(b) as being anticipated by Lanctot et al. (US Patent Application Publication, US 2003/0125258, published Jul. 3, 2003).

The instant claims are drawn to a screening method for a prophylactic/therapeutic substance for a disease involved in differentiation of skeletal muscle cell and/or metabolic abnormality, which comprises bringing a protein comprising an amino acid sequence having an identity of 80%, optionally 90%, or more to the amino acid sequence starting at Amino Acid No. 1 in the amino acid sequence shown by SEQ ID NO:2 or 4, or a salt thereof, into contact with its receptor in the presence or absence of a test substance, and selecting the test substance that changes

the ability of said protein or a salt thereof to bind to said receptor as a candidate for a prophylactic/therapeutic substance for a disease involved in differentiation of skeletal muscle cell and/or metabolic abnormality.

The rejection was stated in the previous office action as it applied to previous claims 31 and 32. In response to this rejection, Applicants have amended claim 31, and added claims 52-54, and traverse the rejection as it applies to the newly amended claims.

Applicants argue that Claim 31 is directed to a **screening method** for a prophylactic/therapeutic substance for a disease involved in differentiation of skeletal muscle cell and/or metabolic abnormality, which comprises bringing a protein comprising an amino acid sequence having an identity of 80% or more to the amino acid sequence starting at Amino Acid No. 1 in the amino acid sequence shown by SEQ ID NO:2 or 4, or a salt thereof, into contact with its receptor in the presence or absence of a test substance, and selecting the test substance that changes the ability of said protein or salt thereof to bind to said receptor as a candidate for a prophylactic/therapeutic substance for a disease involved in differentiation of skeletal muscle cell and/or metabolic abnormality. Applicants further argue that Lanctot et al. neither teach nor suggest the screening method of the instant invention which comprises the steps of selecting a test substance that changes the ability of SS196 or salt thereof to bind to its receptor as a candidate of a prophylactic/therapeutic agent for a disease involved in differentiation of skeletal muscle cell and/or metabolic abnormality. Further, Applicants allege that Lanctot et al. did not disclose that BP-1, which is identical

to SS169 of the present invention, is involved in the regulation of differentiation of skeletal muscle cell and/or metabolic abnormality.

Applicants' arguments have been fully considered but are not deemed persuasive for the following reasons. In the instant case, the active steps of the methods taught by Lanctot et al. are no different from those of Applicants' claimed methods. Further, while the limitation regarding "prophylactic/therapeutic substance" is in reference to the compound that modifies the binding activity of the protein to the receptor, the claim does not recite any active step wherein one selects a compound having the recited functional limitations from any other substances that modulate the binding activity of the protein to the receptor. In fact, the claim states at the end that any compound that changes the binding activity of the protein to the receptor is a candidate for a "prophylactic/therapeutic substance." As such, the methods taught by Lanctot et al. meet the limitations of the claims because the test compound of Lanctot et al. is a candidate for a prophylactic/therapeutic substance according to the last part of the claim. The reference of Lanctot et al. specifically teaches a screening method comprising contacting BP-1 proteins, with a receptor in the presence of a molecule that may modulate binding of BP-1 proteins to a receptor (see paragraph [0144] under "x) Screening Methods Using BP-1 Products"). Further, as previously noted, the secreted human BP-1 protein taught by Lanctot et al. is identical to Applicants' SEQ ID NO: 2 (See SCORE, 20070817_151735_us-10-561-144-2.rag). Therefore, Lanctot et al. anticipate the claimed invention for the reasons provided herein and in the previous office action.

Conclusion

Claims 31, 32 and 52-54 are rejected for the reasons as stated above. Applicants must respond to the objections/rejections in this Office action to be fully responsive in prosecution.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jae W. Lee whose telephone number is 571-272-9949. The examiner can normally be reached on 9-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr Bragdon can be reached on 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/JAE W LEE/

Examiner, Art Unit 1656

/Delia M. Ramirez

Delia M. Ramirez, Ph.D.
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